



Attorney Docket No.: 36290-0416-00-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Patent application of Patrick Gerard :
Johnson *et al.* : Group Art Unit: 1643
Serial No.: 10/580,662 :
Filed: October 10, 2006 : Examiner: Meera Natarajan
For: COMBINATION THERAPY : Confirmation No.: 5029
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PETITION FROM REQUIREMENT OF RESTRICTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

The applicants hereby petition the Director under 37 C.F.R. §§ 1.144 and 1.181 to review the requirement for restriction made in the above-captioned application. The requirement of restriction is based upon a lack of unity finding as between the claims of Group I, consisting of claims 9-17, and the claims of Group II, consisting of claims 18-24. The Group II claims were elected with traverse. The requirement for restriction was made final in the office action mailed August 7, 2008.

No fee is believed due for the present petition, but if any fee is due the Commissioner is authorized to charge deposit account 50-0573.

**CERTIFICATE OF MAILING
UNDER 37 C.F.R. 1.8(a)**

I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date indicated below, with sufficient postage, as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

BY Anissa A. Setzler
Anissa A. Setzler
DATE: December 5, 2008

Introduction

Applicants respectfully file this petition seeking review and withdrawal of the finding of lack of unity, and resulting restriction requirement, as between the claims of

Group I: Claims 9-17, directed to a method killing or treating cancer cells having a p53 mutation, by administration of a therapeutically effective amount of a specific binding member which binds to a cell death receptor or a nucleic acid encoding said binding member, and a chemotherapeutic agent which is a topoisomerase I inhibitor or is pemetrexed; and

Group II: Claims 18-34, directed to a pharmaceutical composition comprising the aforesaid specific binding member or a nucleic acid encoding said binding member, and a chemotherapeutic agent which is a topoisomerase I inhibitor or is pemetrexed; and also a kit containing the specific binding member or nucleic acid encoding the binding member, and a chemotherapeutic agent which is a topoisomerase I inhibitor or is pemetrexed.

Claims Subject to Review

The independent claims of the application, as pending after an Amendment filed on even date, are as follows:

Claims 9 and 10 are the sole independent claims of Group I:

9. A method of killing cancer cells having a p53 mutation, said method comprising the separate, sequential or simultaneous administration to said cells of a therapeutically effective amount of a) an antibody or fragment thereof which binds to the cell death receptor FAS and (b) a chemotherapeutic agent, wherein said chemotherapeutic agent is a topoisomerase I inhibitor.

10. A method of treating cancer cells having a p53 mutation comprising the separate, sequential or simultaneous administration to a mammal in need thereof of a therapeutically effective amount of a) an antibody or fragment thereof which binds to the cell death receptor FAS and (b) a chemotherapeutic agent, wherein said chemotherapeutic agent is a topoisomerase I inhibitor.

Claims 18, 19 and 27 are the independent claims of Group II:

18. A product comprising a) an antibody or fragment thereof which binds to the cell death receptor FAS and (b) a chemotherapeutic agent, for the simultaneous, separate or sequential administration of said antibody or fragment thereof and said chemotherapeutic agent in the treatment of cancer, wherein said chemotherapeutic agent is a topoisomerase I inhibitor, and wherein the cancer cells comprise a p53 mutation.

19. A pharmaceutical composition for the treatment of cancer characterised by the presence of a p53 mutation, wherein the composition comprises a) an antibody or fragment thereof which binds to the cell death receptor FAS and (b) a chemotherapeutic agent, wherein said chemotherapeutic agent is a topoisomerase I inhibitor and (c) a pharmaceutically acceptable excipient, diluent or carrier.

27. A kit for the treatment of a cancer characterised by the presence of a p53 mutation, said kit comprising a) an antibody or fragment thereof which binds to the cell death receptor FAS and (b) a chemotherapeutic agent, wherein said chemotherapeutic agent is a topoisomerase I inhibitor and (c) instructions for the administration of (a) and (b) separately, sequentially or simultaneously.

Procedural History

The finding of disunity as between the above two claim groups was made in the office action mailed November 13, 2007. In a reply filed on April 17, 2008, applicants provisionally elected the claims of Group II, traversing the finding of disunity. Applicants presented arguments in favor of unity.

The Examiner found the arguments of unity unpersuasive, and maintained the requirement of election as between Groups I and II in the office action mailed August 7, 2008. The Group I claims were withdrawn from consideration. The election requirement was made final. The Group II claims were examined on the merits. Applicants filed an Amendment in response to the August 7, 2008 office action on even date with the filing of the herein Petition.

The Action Requested

The Director is respectfully requested to require that the restriction requirement be withdrawn and that all the claims be examined on the merits.

Argument

An applicant may petition from a final requirement for restriction if reconsideration of the requirement was requested. 37 C.F.R. § 1.144. Since applicants' requested reconsideration of the restriction requirement in their response filed April 17, 2008, specifically pointing out the errors in the restriction requirement, and since the restriction requirement was made final in the office action mailed August 7, 2008, the applicants are entitled to petition from the requirement of restriction.

Examiner maintains that Groups I and II do not relate to a single general inventive concept under PCT Article 13.1 because claim 9 allegedly lacks novelty over Allen *et al.*, *Proceedings of the American Research Annual Meeting* 44:418, 2003. It is respectfully submitted that Allen *et al.* does not anticipate claim 9, and therefore does not deprive the unity of invention as between the claims of Groups I and II.

Allen *et al.* describe the effect of 5-FU or TDX together with the CH-11 antibody on Fas-mediated cell death in one specific cell type, the MCF-7 breast cancer cell line. The CH-11 antibody is a specific binding member which binds to a cell death receptor. The MCF-7 cell line is a p53++ cell line. Allen *et al.* explicitly teaches that the effect of 5-FU and TDX in the MCF-7 cells is p53 dependent, indicating that the p53 gene in the MCF-7 line is not mutant.

The Examiner alleged in the August 7, 2008 office action that "it is well known in the art that cancer cells typically have p53 mutations" and "the MCF-7 breast cancer cell line is no exception". In support, Examiner relies on Haldar *et al.*, *Cancer Research*, 54:2095-2097 (1994) as allegedly teaching that the MCF-7 breast cancer cell line has a p53 mutation. However, this allegation by the Examiner is based on a misinterpretation of the teaching of Haldar *et al.*

Haldar *et al.* describes the effect of p53 mutations on bcl-2 function and, as part of the methodology, describes the introduction of a p53 mutation into MCF-7 cells. As taught in paragraph 2, left hand column, of page 2096, introduction of the mutation was achieved by transfecting the eukaryotic vector pc53/Cx22AN into the MCF-7 cell line. According to Haldar *et al.*, vector pc53/Cx22AN expresses a mutant p53 carrying a mutation at codon 175, the same mutation carried by the p53 gene present in the breast cancer cell line SK-BR-3. As explained in the final paragraph of page 2095, SK-BR-3 is a member of a group of cell lines that express high levels of p53 and no bcl-2. In contrast, as explained in the following sentences on the first paragraph of page 2096, MCF-7 is a member of another group of cell lines that express bcl-2 and very little, if any, p53. The latter group includes cells having "no mutation in the p53 gene".

Thus, it is incorrect of the Examiner to state that MCF-7 cells have a mutation in the p53 gene. Haldar *et al.* teaches the contrary, showing that such cells do not carry a p53 mutation. Indeed, they must be transfected with mutant p53 in order to carry mutated p53.

Accordingly, the Examiner is incorrect in the interpretation that Allen *et al.* teaches the technical feature recited in claim 9, *i.e.*, a method of killing cancer cells having a p53 mutation using the recited specific binding member and chemotherapeutic agent. The MCF-7 cells treated in Allen *et al.* do not contain a p53 mutation. Allen *et al.* does not deprive the invention of claim 9 (or claim 10) of novelty. Thus, the basis for the finding of disunity as between the claims of Group I and II is incorrect, and the finding of disunity should be withdrawn.

Claims 9 and 10 do not lack unity over Allen *et al.* for yet another reason. The methods of claims 9 and 10 recite utilization of a chemotherapeutic agent, wherein the chemotherapeutic agent is a topoisomerase I inhibitor. Allen *et al.* describe the effect of 5-FU or TDX together with the CH-11 antibody. Neither 5-FU nor TDX is a topoisomerase I inhibitor. 5-FU is a thymidylate synthase inhibitor, while TDX is a thymidylate synthase inhibitor and antifolate (specification, page 5, lines 10-18). Thus, Allen *et al.* does not defeat the novelty of claims 9 and 10.

Applicants request rejoinder of the claims of Group I with the elected claims of Group II now under examination.

Respectfully submitted,

PATRICK GERARD JOHNSTON *et al.*

BY 
DANIEL A. MONACO
Registration No. 30,480
DRINKER BIDDLE & REATH LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
TEL.: (215) 988-3312
FAX: (215) 988-2757
Attorney for Applicants